REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

Claims 1-13 are pending in the application. Claims 1-5, 7, 8 and 11-13 are amended herein. Basis for the amendments may be found throughout the specification and claims as-filed, especially at page 3. Claim 6 is cancelled. Applicants reserve the right to file at least one continuation or divisional application directed to any subject matter canceled by way of the present Amendment.

Objections under 37 C.F.R. § 1.75(c)

Claims 6-8 and 11-13 stand objected under 37 C.F.R. § 1.75(c) as purportedly in improper form, because a multiple dependent claim cannot serve as the basis for another multiple-dependent claim. Claims 6-8 and 11-13 are amended herein such that no multiple dependent claim serves as the basis for another multiple dependent claim. Thus, the objections are obviated.

Rejections under 35 U.S.C. § 101

Claims 1-5 stand rejected under 35 U.S.C. § 101 because the claimed invention is purportedly directed to non-statutory subject matter as the claims can read on cells that exist within mammals. It appears the Examiner is reading the claim as reciting tumors as existing in humans (*i.e.*, as found in nature), rather than as isolated tumor cells outside the human body. Thus, Applicants submit that the claimed subject matter is not directed to cells that naturally exist in mammals (*i.e.*, in nature). Claim 1 has been amended to recite the subject matter of claim 6, and thus

recites specific combinations of MHC I and MHC II genes not seen in nature. Thus, the claims are not directed to non-statutory subject matter.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1-5, 9, and 10 stand rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite.

The Office Action states that the metes and bounds of claims 1 and 8 cannot be determined. It is purportedly unclear if the limitation of "occurring in humans is to be applied to the origin of the MHC genes, or the origin of the tumor cells, of it "occurring in humans" refers to an analogous occurrence in humans, such as the mouse genes encoding MHC I and II correspond to the HLA genes of humans. Independent claim 1 has been amended to recite the subject matter of claim 6, and thus recites specific combinations of MHC I and MHC II genes. In light of this amendment, Applicants submit that it would be clear to the skilled artisan what is claimed.

Claim 2 is purportedly vague and indefinite in the recitation of "expressed for co-stimulatory molecules". It is purportedly unclear if this phrase indicates that the genes directly express co-stimulatory molecules, or that the expression of the genes indirectly affects the expression of co-stimulatory molecules. Claim 2 is amended herein to clarify that the genes express co-stimulatory molecules, as recited on page 3, last paragraph, of the specification.

It is purportedly unclear if the metes and bounds of claim 3 entails the expression of both B7 and CD44, or if either B7 or CD44 are expressed. Claim 3 is amended herein to clarify that B7 and CD44 are alternatives.

Claim 4 stands rejected as purportedly vague and indefinite in the recitation of "expressed for cytokines". It is purportedly unclear if this indicates that the genes directly express the cytokines, or that the expression of the genes indirectly affects the expression of cytokines. Claim 4 is amended herein to clarify that the genes express cytokines, as recited on page 3, last paragraph, of the specification.

It is purportedly unclear if the metes and bounds of claim 5 entails the expression of all of interleukins, GM-CSF, TNF-alpha and interferon-gamma, or if either interleukins, GM-CSF, TNF-alpha or interferon-gamma are expressed. Claim 5 is amended herein to clarify that the listed cytokines in the tumor cells are alternatives.

It is purportedly unclear as to how the first active method step of claim 9, "tissue typing of tumor cells" relates to the method objective or producing tumor cells according to claim 1, or to the subsequent active method steps in claim 9. Applicants submit the meaning of claim 1 would be clear to the skilled artisan in light of the specification. Step (a) of claim 9 is discussed in the specification in Example B, which states that before modification of the tumor cells, it must be clarified whether the cells are, for example, normal lymphocytes or tumor cells. The modification is accomplished by introducing MHC I and/or MHC II genes and/or genes encoding co-stimulatory molecules. *See* the specification, page 7. Thus, it is clear that "tissue typing of tumor cells" is a prerequisite for carrying out the further method steps (b) and (c) of claim 9.

In light of the above amendments and remarks, Applicants request that the 35 rejections under 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C. § 102

Claims 1 and 9 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Ostrand-Rosenburg et al. (*Journal of Immunogenics*, 16: 343-349 (1989)). Ostrand-Rosenburg et al. purportedly disclose a murine sarcoma cell transfected to express syngenic IAk. Ostrand-Rosenburg et al. purportedly also disclose that the Sal tumor is H-2a, KkDd before transfection.

"[A]nticipation requires the presence in a single prior art disclosure of all elements of a claimed invention as arranged in the claims." *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 225 U.S.P.Q. 253, 256 (Fed. Cir. 1985). The cited reference fails to describe or even suggest all of the elements of the rejected claims.

Independent claim 1 has been amended to recite the subject matter of claim 6, including specific combinations of MHC I genes and MHC II genes. These combinations are not recited in Ostrand-Rosenburg et al. Thus, Ostrand-Rosenburg et al. do note recite each element of the claims.

Claims 1-3, 9 and 10 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Lindauer et al. (*Immunology*, 93: 390-97 (1998)) or Kerkmann-Tucek et al. (*International Journal of Cancer*, 77: 114-122 (1998). Lindauer et al. purportedly disclose the human colorectal tumor cell, SW480), transfected with HLA-DR (MHC II) and B7 (CD/80/CD86) Kerkmann-Tucek et al. purportedly disclose a murine RENCA tumor cell transfected to express both MHC class II and B7.

Independent claim 1 has been amended to recite the subject matter of claim 6, including specific combinations of MHC I genes and MHC II genes. These

combinations are not recited in Kerkmann-Tucek et al. or Lindauer et al. Thus, the cited references do note recite each element of the claims.

Claims 1-3 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Dessureault et al. (*Journal of Surgical Research*, 64: 42-48 (1996)). Dessureault et al. purportedly disclose melanoma cells transfected with the B7.1 co-stimulatory molecule. Independent claim 1 has been amended to recite the subject matter of claim 6, including specific combinations of MHC I genes and MHC II genes. These combinations are not recited in Dessureault et al. Thus, Dessureault et al. do note recite each element of the claims.

Claims 1-5, 9 and 10 stand rejected under 35 U.S.C. § 102(e) as purportedly anticipated by Ostrand-Rosenburg et al. (U.S. Patent No. 5,858,776). Ostrand-Rosenburg et al. purportedly disclose tumor cells transfected with B7, MHC class I, MHC class II and cytokines , that the tumor cells are from a human patient and that interferon-gamma is a preferred cytokine. Independent claim 1 has been amended to recite the subject matter of claim 6, including specific combinations of MHC I genes and MHC II genes. These combinations are not recited in Ostrand-Rosenburg et al. Thus, Ostrand-Rosenburg et al. do note recite each element of the claims.

Rejections under 35 U.S.C. § 103

Claims 1-5, 9, and 10 stand rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Lindauer et al. in view of Abdel-Wahab et al. (Cancer, 80: 401-412 (1997)). Lindauer et al. purportedly disclose tumor cells expressing, MHC I and MHC II and B7, wherein said tumor cells are made by transfections of the genes

encoding MHC II and B7. Abdel-Wahab et al. purportedly disclose that the immunization of mice with mouse tumor cells transduced to express cytokines induced a strong immune response against a mouse tumor. The Office Action states that it would purportedly have been obvious to the skilled artisan to transfect the tumor cells of Lindauer et al. to express interferon-gamma in addition to MHC II and B7.

As set forth in M.P.E.P 2142, in order to establish a *prima facie* case of obviousness, three criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art references must teach or suggest all the claim limitations. The cited reference fails to meet these requirements. Independent claim 1 has been amended to recite the subject matter of claim 6, including specific combinations of MHC I genes and MHC II genes. These combinations are not recited in Lindauer et al. or Abdel-Wahab et al. Nor do either of the references, alone or in combination provide any suggestion of these combinations of genes, or motivation to arrive at these combinations.

Claims 3, 9 and 10 stand rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Dessaureault et al. in view of Ostrand-Rosenburg et al. Dessurealut et al. purportedly disclose the specific embodiments which anticipate claims 1-3. Ostrand-Rosenburg et al. purportedly disclose the transfection of a mouse tumor cell with IAk resulting in the expression of both MHC class I and MHC

class II. The Office Action states that it would have been obvious to the skilled artisan to transfect the allogenic MHC I and MHC II genes into melanoma cells which were MHC class I negative and MHC class II negative in addition to the B7 gene. Applicant is traverse.

Independent claim 1 has been amended to recite the subject matter of claim 6, including specific combinations of MHC I genes and MHC II genes. These combinations are not recited in Dessaureault et al. or Ostrand-Rosenburg et al. Nor do the references, alone or in combination, provide any suggestion of these combinations of genes, or any motivation to arrive at these combinations.

Claims 1-5, 9 and 10 stand rejected under 35 U.S.C. § 103 (a) as purportedly unpatentable over Dessuaureault et al. and Ostrand-Rosenburg et al. as applied to claims 1-3, 9 and 10 above in further view of Abdel-Wahab.

Abdel-Wahab et al. purportedly disclose that immunization of mice with mouse tumor cells transduced to express cytokines induced a strong immune response against a mouse tumor. The Office Action states that it would have been obvious to transfect the tumor cells of to transfect tumor cells with genes encoding B7, MHC in addition to the genes encoding cytokines, especially interferon-gamma.

Independent claim 1 has been amended to recite the subject matter of claim 6, including specific combinations of MHC I genes and MHC II genes. These combinations are not recited in Dessaureault et al., Ostrand-Rosenburg et al. or Abdel-Wahab. Nor do these references, alone or in combination, provide any suggestion of these combinations of genes, or motivation to arrive at these combinations. To this end, the secondary reference, Abdel-Wahab, fails to remedy the deficiencies of Dessaureault et al. and Ostrand-Rosenburg et al.

In light of the amendments herein, Applicants request that these rejections be withdrawn.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

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Date: June 14, 2004

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